

CLAIMS

1. A modified siRNA comprising a sense strand and an antisense strand, wherein the sense strand comprises a modified RNA nucleotide in at least one of positions 8-14, calculated from the 5'-end.

2. The modified siRNA according to claim 1, wherein the sense strand comprises a modified RNA nucleotide in at least one position selected from the group consisting of position 8, position 9, position 10, position 11, position 12, position 13 and position 14, calculated from the 5'-end.

3. The modified siRNA according to claim 1 or 2, wherein said modified RNA nucleotide comprises a modification selected from the group consisting of a non-RNA nucleobase, a sugar moiety which differs from ribose, an internucleoside linkage group which differs from phosphate, and combinations thereof.

4. The modified siRNA according to claim 3, wherein said modified RNA nucleotide comprises a non-RNA nucleobase.

5. The modified siRNA according to claim 4, wherein the sense strand comprises a non-RNA nucleobase in at least one position selected from the group consisting of position 9, position 10, position 11, position 12 and position 13, calculated from the 5'-end.

6. The modified siRNA according to claim 5, wherein the sense strand comprises a non-RNA nucleobase in a position selected from the group consisting of position 10, position 11 and both of positions 10 and 11, calculated from the 5'-end.

7. The modified siRNA according to claim 6, wherein the sense strand comprises a non-RNA nucleobase in position 10, calculated from the 5'-end.

8. The modified siRNA according to any of claims 4-7, wherein said non-RNA nucleobase is selected from the group consisting of thymine (T), 5-methylcytosine (^{Me}C), isocytosine, pseudoisocytosine, 5-bromouracil, 5-propynyluracil, 5-propyny-6-fluoroluracil, 5-methylthiazoleuracil, 6-aminopurine, 2-aminopurine, inosine, 2,6-diaminopurine, 7-propyne-7-deazaadenine, 7-propyne-7-deazaguanine and 2-chloro-6-aminopurine.

9. The modified siRNA according to claim 8, wherein said non-RNA nucleobase is T or ^{Me}C.

10. The modified siRNA according to claim 9, wherein said non-RNA nucleobase is T.

5 11. The modified siRNA according to claim 3, wherein said modified RNA nucleotide comprises a sugar moiety which differs from ribose.

12. The modified siRNA according to claim 11, wherein the sense strand comprises a sugar moiety which differs from ribose, in at least one position selected from the group consisting of
10 position 9, position 10, position 11, position 12 and position 13, calculated from the 5'-end.

13. The modified siRNA according to claim 12, wherein the sense strand comprises a sugar moiety which differs from ribose, in at least one position selected from the group consisting of position 11, position 12 and position 13, calculated from the 5'-end.

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14. The modified siRNA according to claim 13, wherein the sense strand comprises a sugar moiety which differs from ribose in position 12, calculated from the 5'-end.

15. The modified siRNA according to any of claims 11-14, wherein said sugar moiety differs
20 from ribose in that the ribose 2'-OH group has been modified.

16. The modified siRNA according to claim 15, wherein said sugar moiety is LNA.

17. The modified siRNA according to claim 16, wherein said LNA is selected from the group
25 consisting of thio-LNA, amino-LNA, oxy-LNA and ena-LNA.

18. The modified siRNA according to claim 17, wherein said LNA is oxy-LNA.

19. The modified siRNA according to claim 18, wherein said oxy-LNA is in the beta-D form.
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20. The modified siRNA according to claim 3, wherein said modified RNA nucleotide comprises an internucleoside linkage group which differs from phosphate.

21. The modified siRNA according to claim 20, wherein the sense strand comprises an
35 internucleoside linkage group which differs from phosphate, in at least one position selected

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from the group consisting of position 9, position 10, position 11, position 12 and position 13, calculated from the 5'-end.

22. The modified siRNA according to claim 21, wherein the sense strand comprises an internucleoside linkage group which differs from phosphate, in at least one position selected from the group consisting of position 11, position 12 and position 13, calculated from the 5'-end.

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23. The modified siRNA according to claim 22, wherein the sense strand comprises an internucleoside linkage group which differs from phosphate in position 12, calculated from the 5'-end.

10 24. The modified siRNA according to any of claims 20-23, wherein said internucleoside linkage group which differs from phosphate is phosphorothioate (-O-P(O,S)-O-).

25. The modified siRNA according to any of the preceding claims, wherein at least one of the strands further comprises at least one modified RNA nucleotide.

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26. The modified siRNA according to any of the preceding claims, wherein the sense strand comprises a sugar moiety which differs from ribose in position 12, calculated from the 5'-end, and wherein the sense strand comprises a non-RNA nucleobase in position 10, calculated from the 5'-end.

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27. The modified siRNA according to any of the preceding claims, wherein each strand comprises 12-35 monomers.

25 28. A pharmaceutical composition comprising the modified siRNA as defined in any of claims 1-27 and a pharmaceutically acceptable diluent, carrier or adjuvant.

29. The modified siRNA according to any of claims 1-27 for use as a medicament.